

**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

1.(original) An aqueous solution suitable for intranasal administration, which comprises from 0.1 to 10 mg/ml of buprenorphine or a physiologically acceptable salt or ester thereof and from 5 to 40 mg/ml of a pectin having a degree of esterification of less than 50%; which solution has a pH of from 3 to 4.2, is substantially free from divalent metal ions and gels on the nasal mucosa.

2.(original) A solution according to claim 1, wherein the buprenorphine or buprenorphine salt or ester is present in an amount of from 0.5 to 8 mg/ml.

3.(original) A solution according to claim 2, wherein the buprenorphine or buprenorphine salt or ester is present in an amount of from 1 to 6 mg/ml calculated as buprenorphine.

4.(previously presented) A solution according to claim 1, which comprises buprenorphine hydrochloride.

5.(previously presented) A solution according to claim 1, wherein the pectin is present in an amount of from 10 to 30 mg/ml.

6.(previously presented) A solution according to claim 1, wherein the pectin has a degree of esterification of from 10 to 35%.

7.(previously presented) A solution according to claim 1, wherein the pH is from 3.5 to 4.0.

8.(previously presented) A solution according to claim 1, wherein the pH has been adjusted by means of hydrochloric acid.

9.(previously presented) A solution according to claim 1, which comprises a preservative.

10.(original) A solution according to claim 9, which comprises phenylethyl alcohol and propyl hydroxybenzoate as preservatives.

11.(previously presented) A solution according to claim 1, which has an osmolality of from 0.35 to 0.5 osmol/kg.

12.(previously presented) A solution according to claim 1, which contains dextrose as a tonicity adjustment agent.

13.(original) An aqueous solution suitable for intranasal administration, which has a pH of from 3.5 to 4.0, which is substantially free from divalent metal ions and which comprises:

- (a) from 1 to 6 mg/ml of buprenorphine or a physiologically acceptable salt or ester thereof, calculated as buprenorphine,
- (b) from 10 to 40 mg/ml of a pectin which has a degree of esterification from 10 to 35%, and
- (c) dextrose as a tonicity adjustment agent.

14.(original) A process for the preparation of an aqueous solution as defined in claim 1, which process comprises dissolving buprenorphine or a physiologically acceptable salt or ester thereof in water; mixing the resulting solution with a solution in water of a pectin having a degree of esterification of less than 50% such that the mixed solution comprises from 0.1 to 10 mg/ml of buprenorphine or said salt or ester thereof and from 5 to 40 mg/ml of the pectin; and adjusting the pH of the solution to a value from 3 to 4.2 if desired.

15.(original) A process according to claim 14, wherein the resulting solution is introduced into a nasal delivery device.

16.(original) An aqueous solution suitable for intranasal administration, which comprises:

- (a) from 0.1 to 10 mg/ml of buprenorphine or a physiologically acceptable salt or ester thereof,
  - (b) from 0.1 to 20 mg/ml of a chitosan, and
  - (c) from 0.1 to 15 mg/ml of hydroxypropylmethylcellulose;
- which solution has a pH of from 3 to 4.8.

Claim 17-18 (Cancelled).

19.(original) An aqueous solution suitable for intranasal administration, which comprises:

- (a) from 0.1 to 10 mg/ml of buprenorphine or a physiologically acceptable salt or ester thereof,
  - (b) from 0.1 to 20 mg/ml of a chitosan, and
  - (c) from 50 to 200 mg/ml of a polyoxyethylene-polyoxypropylene copolymer of the general formula  $\text{HO}(\text{C}_2\text{H}_4\text{O})_a(\text{C}_3\text{H}_6\text{O})_b(\text{C}_2\text{H}_4\text{O})_a\text{H}$  wherein a is from 2 to 130 and b is from 15 to 67;
- which solution has a pH of from 3 to 4.8.

Claims 20 -37 (Cancelled).

38.(previously presented) A nasal delivery device loaded with a solution as claimed in claim 1.

39.(original) A device according to claim 38, which is a spray device.

Claim 40 (Cancelled).

41.(previously presented) A method of inducing analgesia in a patient in need thereof, which method comprises intranasally administering an aqueous solution as defined in claim 1.

Claims 42-47 (Cancelled).

48.(currently amended) A pharmaceutical composition suitable for use as an analgesia which comprises buprenorphine or a physiologically acceptable salt or ester thereof and a delivery agent whereby, on introduction into the nasal cavity of a patient to be treated, the buprenorphine or salt or ester thereof is delivered to the bloodstream to produce within 0.5 to 20 minutes a therapeutic plasma concentration  $C_{ther}$  of 0.4 to 5 ng/ml or greater which is maintained for a duration  $T_{maint}$  ~~of at least 2 hours~~ is at least 6 hours.

49.(currently amended) A method of inducing analgesia in a patient in need thereof, which method comprises administering intranasally to said patient a pharmaceutical composition which comprises buprenorphine or a physiologically acceptable salt or ester thereof and a delivery agent whereby, on introduction into the nasal cavity of said patient to be treated, the buprenorphine or salt or ester thereof is delivered to the bloodstream to produce within 0.5 to 20 minutes a therapeutic plasma concentration  $C_{ther}$  of 0.4 to 5ng/ml or greater which is maintained for a duration  $T_{maint}$  ~~of at least 2 hours~~ is at least 6 hours.

50.(original) A method according to claim 49, wherein a unit dosage of 0.1 to 0.6 mg of buprenorphine or buprenorphine salt or ester, calculated as buprenorphine, is administered intranasally.

51.(currently amended) A method according to claim ~~49~~48, wherein ~~the a~~ a ~~therapeutic plasma concentration  $C_{ther}$  of 0.4 ng/ml or more is produced within 2 to 15 minutes~~ therapeutic plasma concentration  $C_{ther}$  of 0.4 ng/ml or more is produced within 2 to 15 minutes ~~and is maintained for a duration  $T_{main}$  of 2 to 4~~ is from 6 to 12 hours.

52.(currently amended) A pharmaceutical composition according to claim 4849, wherein ~~a therapeutic plasma concentration  $C_{ther}$  of 0.4 ng/ml or more is produced within 2 to 15 minutes and is maintained for a duration  $T_{main}$  of 2 to 4~~ is from 6 to 12 hours.

53.(previously presented) A solution according to claim 16, wherein the buprenorphine or buprenorphine salt or ester is present in an amount of from 0.5 to 8 mg/ml.

54.(previously presented) A solution according to claim 53, wherein the buprenorphine or buprenorphine salt or ester is present in an amount of from 1 to 6 mg/ml calculated as buprenorphine.

55.(previously presented) A solution according to claim 16, which comprises buprenorphine hydrochloride.

56.(previously presented) A process for the preparation of an aqueous solution as defined in claim 16, which process comprises dissolving buprenorphine or a physiologically acceptable salt or ester thereof, a chitosan and HPMC in water to provide a solution comprising from 0.1 to 10 mg/ml of buprenorphine or said salt or ester thereof, from 0.1 to 20 mg/ml of chitosan and from 0.1 to 15 mg/ml of HPMC; and adjusting the pH of the solution to a value from 3 to 4.8 as desired.

57.(previously presented) A nasal delivery device which comprises an aqueous solution as defined by claim 16.

58.(previously presented) A nasal delivery device according to claim 57 which is a spray device.

59.(previously presented) A method of inducing analgesia in a patient in need thereof, which method comprises intranasally administering an aqueous solution as defined in claim 16.

60.(previously presented) A solution according to claim 19, wherein the buprenorphine or buprenorphine salt or ester is present in an amount of from 0.5 to 8 mg/ml.

61.(previously presented) A solution according to claim 62, wherein the buprenorphine or buprenorphine salt or ester is present in an amount of from 1 to 6 mg/ml calculated as buprenorphine.

62.(previously presented) A solution according to claim 19, which comprises buprenorphine hydrochloride.

63.(previously presented) A process for the preparation of an aqueous solution as defined in claim 19, which process comprises dissolving buprenorphine or a physiologically acceptable salt or ester thereof, a chitosan and a polyoxyethylene-polyoxypropylene copolymer of the general formula  $\text{HO}(\text{C}_2\text{H}_4\text{O})_a (\text{C}_3\text{H}_6\text{O})_b (\text{C}_2\text{H}_4\text{O})_a\text{H}$  wherein a is from 2 to 130 and b is from 15 to 67, in water to provide a solution comprising from 0.1 to 10 mg/ml of buprenorphine or said salt or ester thereof, from 0.1 to 20 mg/ml of chitosan and from 50 to 200 mg/ml of the polyoxyethylene-polyoxypropylene copolymer; and adjusting the pH of the solution to a value from 3 to 4.8 as desired.

64.(previously presented) A nasal delivery device which comprises an aqueous solution as defined by claim 19.

65.(previously presented) A nasal delivery device according to claim 64 which is a spray device.

66. (previously presented) A method of inducing analgesia in a patient in need thereof, which method comprises intranasally administering an aqueous solution as defined in claim 19.